KINETICS OF THE DECOMPOSITION OF RIBOSE AND OTHER SUGARS: IMPLICATIONS FOR CHEMICAL EVOLUTION

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The idea of a RNA world (7, 16), in which RNA acts both as catalyst and informational macromolecule (18, 3, 13), assumes a large prebiotic source of ribose or the existence of pre-RNA molecules with backbones different from ribose-phosphate. The generally accepted prebiotic synthesis of ribose, the formose or Butlerow reaction, produces almost all possible pentoses and hexoses, including branched chain sugars, without any selectivity (4, 15). Even if there were a selective synthesis of ribose, there is still the problem of its stability. Sugars are known to be unstable in strong acid or base (5, 6, 8, 10, 14), but there are few data for neutral solutions (2, 11). Therefore, following sugar concentration by ^{1}H-NMR, we have measured the rate of decomposition of ribose at various conditions between pH 4 and 8 (converted to pD by the formula pD = pH + 0.4 (1)) from 40°C to 120°C (Figure 1). Ribose decomposition is a first order reaction and the rate is approximately proportional to the [OD^-] in the pD range 4 to 6. The rate is faster than extrapolated from Figure 1 at pD < 4 due to acid catalysis (not shown). The curve levels off at higher pH values, suggesting that the ionization of an intermediate in the decomposition is the rate determining step although it could also be due to general base catalysis by HPO_4^{-2} rather than OH^- (to minimize posible catalysis by the buffer, the lowest buffer concentration that maintained the pH at a constant value was used: 0.05 M phosphate or acetate). Although phosphate is a minor component in the present ocean, there is considerable buffering by the 2.3 x10^{-3} M HCO_3^-. The bicarbonate concentration would have been higher in a prebiotic ocean with a primitive atmosphere high in CO_2 (17, 9). We measured the rate of ribose decomposition at pD 7.4 using a 0.05 M bicarbonate buffer and the rate is 0.52 that of a 0.05 M phosphate buffer. We believe therefore, that these results should be applicable to any reasonable primitive ocean model.

The ribose half-lives are so short that it is difficult to see how it could have played a role in any high temperature origin of life scenario (73 minutes at pH 7.0 and 100°C,). The temperature dependence of the rate of ribose decomposition follows an Arrhenius curve given by $\log k\ (s^{-1}) = 11.23 - 5608/T$ (pD 7.4) with a heat of activation of 25.7 kcal mol^{-1}. The half-life at pD 7.4 extrapolates to 300 days at 25°C and 44 years at 0°C, so is not clear how ribose could have been available for prebiotic use, even at low temperatures.

The stability of other sugars is of interest not only for their involvement in many biological processes, but because they may have been utilized earlier than ribose. The other aldopentoses and aldohexoses have half lives within an order of magnitude of the ribose values, at pH 7.0 and 100°C, as do 2-deoxyribose, ribose-5-phosphate and ribose-2,4-diphosphate. Unless the temperature coefficients of these decompositions differ greatly from that of ribose, it is clear that these other sugars are as unlikely as ribose to have been available in the prebiotic world.

Given the existence of a variety of other decomposition pathways, like Maillard and Kiliani reactions, these data probably underestimate the rate of decomposition of sugars under plausible prebiotic conditions, making it unlikely that they played a role in early prebiotic syntheses.

The above results show that stability considerations preclude the use of ribose and other sugars as prebiotic reagents except under very special conditions. It follows that ribose and other sugars were not components of the first genetic material, and that other possibilities, such as the peptide nucleic acids (12) and other non-sugar based backbones, should be examined.

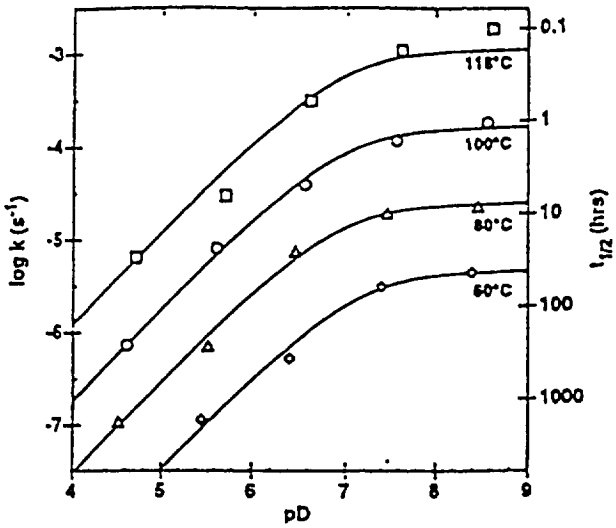

FIG. 1. Rates of ribose decomposition as a function of pD. The curves were fitted by assuming a functional form $k = k_0/(1 + [H^+]/K_a)$, where K_a and k_0 are adjusted constants.

1. Bates, R.G. :1964, *Determination of pH: Theory and Practice*, 2nd ed ,Wiley, NY.
2. Borenfreund, E. and Dische, Z. : 1957, *Biochim. Biophys. Acta* 25, 215-216.
3. Crick, F.H.C. : 1968, *J. Mol. Biol.* 38, 367-379.
4. Decker, P. et al. : 1982, *J. Chromatog.* 244, 281-291.
5. El Khadem, H.S.et al. : 1987, *Carbohyd. Res.* 169, 13-21.
6. Evans, W.L. : 1942, *Chem. Rev.* 31, 537-560.
7. Gilbert, W. : 1986, *Nature* 319, 618.
8. Isbell, H.S. et al. : 1969, *Carbohyd. Res.* 9, 163-175.
9. Kasting, J. F. (1993) *Science* 259, 920-926.
10. Khym, J. X. et al. : 1954, *J. Am. Chem. Soc.* 76, 5523-5530.
11. Mopper, K. et al. : 1980, *J. Marine Chemistry* 10, 55-66.
12. Nielsen, P.E. : 1993, *Orig. Life Evol. Biosph.* 23, 323-327.
13. Orgel, L.E. : 1968, *J. Mol. Biol.* 38, 381-393.
14. Pigman, W. and Anet, E.F.L.J. : 1972, in *The Carbohydrates: Chemistry and Biochemistry* 2nd ed., Academic Press, NY, vol 14, pp. 165-194.
15. Shapiro, R. : 1988, *Orig. Life Evol. Biosph.* 18, 71-85.
16. Sharp, P.A. : 1985, *Cell* 42, 397-400.
17. Walker, J. C. G. (1983) *Nature* 302, 518-520.
18. Woese, C. : 1967,*The Genetic Code* , Harper & Row, New York, pp. 179-195.

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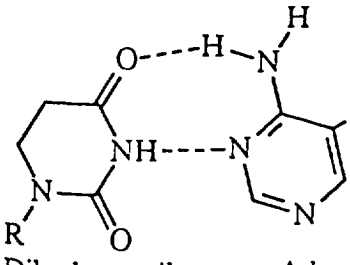

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